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VINCENT A. KLEINFELD
1907-1993

October 6, 1999

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

Re: Docket No. 99P- 1589: Additional Reply of Purdue Pharma L.P. to Roxane Laboratories' Submission of September 23, 1999

Dear Sir/Madam:

We respond to only two points Roxane has raised in its September 23, 1999 filing. We will allow our prior filings to speak for themselves on the other issues.

(1) Roxane cites certain comments of the FDA Statistical Reviewer in an attempt to establish that its "pivotal" efficacy studies can stand on their own. Roxane ignores, however, that these comments conflict with the reviewer's conclusion that the Roxane studies provided no statistically valid evidence of effectiveness. (See SBA, Statistical Review and Evaluation, page 22; see also Purdue's August 20, 1999 submission, pages 2-3.)

The comments cited by Roxane rely on the view that "it would be hard to believe" the efficacy profiles in the Roxane studies would have been seen if Roxicodone™ SR were simply a "placebo." This non-statistically based comment could just as well have been made if the Roxane studies had never been done, e.g., "What are the chances that a product with a large amount of oxycodone in it will not be an effective pain reliever?" However, FDA regulations and statutory requirements for "substantial evidence" of effectiveness require clinical efficacy studies to be conducted and require the adequacy of those clinical studies to be

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determined by statistical criteria and not by "eyeballing" the results. The Roxane studies failed to provide such statistically valid proof of efficacy of Roxicodone™ SR.

Accordingly, Purdue's request for relief – that FDA declare the purported approval of Roxane's NDA as a §505(b)(1) application to be null and void – is buttressed (not changed) by the inadequacy of Roxane's effectiveness data. The only way FDA could have properly approved Roxane's NDA is for FDA and Roxane to have relied on investigations regarding effectiveness conducted by others (such as Purdue's statistically valid, placebo and active-controlled efficacy studies of OxyContin®), to which Roxane did not have a right of reference. Reliance on such investigations requires the determination that the Roxane application should have been submitted by Roxane and processed by FDA as a $505(b)(2) application.'

(2) On page 5 of its September 23 filing, Roxane states:

> Not all information in an NDA is an investigation described in Section 505(b)(l)(A). No right of reference to information that is instead submitted in support of the requirements that the labeling of a drug should be truthful and informative – see Sections 505(b)(l)(F) and (d)(7) – is required to avoid Section 505(b)(2) status.

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[1] For these same reasons, Purdue's citation to serious deficiencies in the approved Roxicodone™ SR labeling, e.g., that the "approved" labeling of the Roxicodone™ SR product is materially false and misleading with regard to teratogenicity and mutagenicity tests (another fact which Roxane has made no attempt to refute), does not change the relief Purdue seeks and is entitled to under the law. As Purdue explained fully in its July 19, 1999 submission, those deficiencies underscore the fact that the issues involved in the 505(b)(1) or (b)(2) classification of the Roxane application were not properly handled in the submission or review of that application. While it is true that those same deficiencies would also preclude marketing of the Roxicodone™ SR product even if the approval had been legally issued (since such marketing would violate the general misbranding provisions of the FFDCA), Purdue is nevertheless entitled to the declaration, sought in its Citizen Petition, that the Roxicodone™ SR "approval" is legally void as having been issued in contravention of Purdue's statutory patent and non-patent exclusivity rights.

On this basis, Roxane would have FDA ignore the fact that the Roxicodone™ SR labeling is clearly based, in significant part, on data from studies to which Roxane has no right of reference.[2] But Roxane is wrong. While the requirement to submit draft labeling appears, as Roxane cites, under a different statutory provision, the data required to support that labeling can be submitted or referenced only under §505(b)(1)(A).[3] Appropriate exclusivity restrictions therefore apply to an application that relies for approval of the drug and its labeling on data to which there is no right of reference. Here, as Purdue has previously outlined in detail, Roxane's application relies on unauthorized data in both of these interrelated contexts.

* * * * *

In all of its submissions to this Docket, Roxane has yet to suggest any substantive basis for FDA to find that the approval of the Roxicodone™ SR application was properly issued during applicable and continuing exclusivity periods for Purdue's OxyContin® Tablets. Moreover, to the large extent that Roxane's apparent defense is based on its demand for a §505(e) hearing on the "withdrawal" of an approval that was void *ab initio*, Roxane would compound the harm to Purdue and to FDA that arises out of its efforts to circumvent Purdue's patent and non-patent exclusivity rights. As Purdue explained fully in its previous tilings, FDA has the right and the duty to declare as void an "approval" that has

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[2] After at least three submissions to this docket, Roxane still appears effectively to concede this and other facts central to Purdue's position despite Roxane's confusing and disingenuous refusal to admit that it has done so. (See Purdue's August 20, 1999 submission.)

[3] Section 505(b)(l)(A) requires the submission of:

> full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use. , . .

There is no other provision of the FFDCA (including both $505(b)(l)(F) and §505(d)(7)) which provides for the submission of data to support the safety and effectiveness of a drug under the conditions of use set out in proposed, draft labeling submitted under §505(b)(l)(F).

been illegally issued in violation of Purdue's statutory rights, and should proceed to do so now.

Respectfully submitted,

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